AMENDMENTS TO THE SPECIFICATION:

Please amend the specification as follows:

Please replace the paragraph beginning at page 7, line 13, with the following paragraph:

In accordance with yet another aspect of the invention, a fluid handling device for aspirating reagents is disclosed. The device preferably includes a reagent manifold that comprises an aspiration chamber, two or more reagent input lines, a gas input line, a reagent manifold sealing surface and a movable probe. The aspiration chamber diameter is preferably larger than the probe diameter and the aspiration chamber height is preferably substantially the same as the probe height. In an embodiment of the present invention, the aspiration chamber diameter is 25% larger than the probe diameter. The aspiration chamber preferably has an access port and is ~~defined~~ provided within the reagent manifold. The plurality of reagent input lines are preferably arranged at substantially the same height and the gas input line is preferably arranged above the reagent input lines. The reagent input and gas input lines are preferably adapted to be in selective fluid communication with the aspiration chamber. The movable probe includes a probe tip and preferably a probe sealing surface that is adapted to sealingly engage the reagent manifold sealing surface when the probe is lowered into the aspiration chamber. In another embodiment, a seal configured to enclose the access port and to form a face seal when the probe is lowered into the aspiration chamber is employed. The seal can be a an o-ring, a gasket, or an elastomeric material and can be either arranged on the probe sealing surface or the reagent manifold sealing surface. The seal is preferably arranged within a groove of the appropriate sealing surface.

Please replace the paragraph beginning at page 12, line 17, with the following paragraph:

Figs. 3a-l ~~**, 3a-2, ...,**~~ through **3a-10** illustrate several suitable geometries of alignment features useful for calibrating the position of a fluidic probe.

Please replace the paragraph beginning at page 15, line 3, with the following paragraph:

Various automation systems may be employed such as a plate loader for facilitating proper loading of sample carriers and a pipettor (preferably, a movable pipettor under automated control) for aspirating/dispensing fluids from one or more locations within the system. The plate loader **110** depicted in **Fig. 1a** is a simple one degree of freedom device that translates a plate linearly from one position (typically outside of the biological detection system's housing) to a second position (typically inside the biological detection system's housing) but may optionally be adapted to have additional degrees of freedom in the vertical direction or in the plane of the plate. The system, however, is not limited to such a plate loader and may utilize any system capable of transporting the sample carrier from a loading point to a point where the carrier is positioned for processing by the system; e.g., a rotary system could be employed wherein the sample carrier is loaded on an arm that rotationally pivots about some point. The automated pipettor **405**, including probe **150**, as shown in **Fig. 1a** is capable of motion in 3-dimensions within a Cartesian coordinate system through three independently controllable motors ~~**175, 166, 177,**~~ however, motion control systems based on alternative coordinate systems may be used (e.g., one dimensional, two dimensional, polar coordinates, etc.). The independent controllable motors may, for example, comprise y-axis actuator **175**, x-axis actuator **176**, and z-axis actuator **177**, as illustrated in **Fig. 1a**. Operation of the automation systems are preferably controlled by a motion control subsystem. As depicted, the motion control subsystem **102** preferably receives

instructions from the computerized system **101** which it then converts into appropriate control signals that direct one or more of the automation systems to perform the necessary steps to carry out the computerized system's instructions.

Please replace the paragraph beginning at page 16, line 1, with the following paragraph:

The flow-cell based biological detection system may also comprise a fluid handling station for introducing reagents and/or samples that may include gases and liquids. **Fig. 1a** depicts fluid handling ~~station~~ device **471** that comprises flow control valves **470**, reagent/gas detectors **500** and a fluid handling ~~manifold~~ system **425**. These devices may be independent fixtures fluidically connected (e.g., through flexible tubing) or may be integrated into a single system (as indicated by the dashed line). In an alternative embodiment, the location of valves **470** and sensors **500** along the fluidic lines is switched so that sensors **500** are between reagent bottles **472** and valves **470**. The fluid handling ~~manifold~~ system **425** preferably includes an aspiration chamber **450** employing a face-sealing configuration, e.g., using an o-ring **415** arranged on a sealing surface of the manifold, that is adapted to achieve a fluidic seal between the manifold and a sealing surface **410** of the pipettor **405** (e.g., a collar, flange, or the like). Pipettor **405** is connected to z-axis actuator **177** and may comprise a sealing surface **410** and a probe **150**. Probe **150** may comprise a needle probe having a tip. As depicted, the fluid handling manifold sealing surface is preferably located away from the reagent input lines (e.g., above the reagent lines' aspiration chamber entry points). Additionally, one or more of the reagent entry points can be positioned at predetermined heights within the aspiration chamber; e.g., as depicted, the liquid reagent lines can be positioned beneath the gas reagent lines to preclude contamination of the gas lines. Reagent aspiration is preferably controlled by coordinating the

selective actuation of one or more of the reagent valves **470** with the proper positioning of the pipettor and activation of the pump **870** so as to draw the reagents from the selected reagent bottles **472**. Reagent detectors **500** can be employed to determine the presence and/or absence of reagent (e.g., whether one or more of reagent bottles **472** are empty), determine the presence and/or absence of gaseous reagents (e.g., when air is used to segment fluids as they are aspirated), determine/confirm the aspirated volume of a particular reagent, etc.

Please replace the paragraph beginning at page 19, line 6, with the following paragraph:

In operation, plate loader **110** loads sample carrier **115** (e.g., a microtiter plate) and properly aligns it within the biological detection system through the use of positioning blocks **130** and **140** and positioning stop **120**. Detector **200** determines if the plate is correctly positioned. Pipettor **405**, under the control of motion control system **102**, is positioned in fluid handling ~~manifold~~ system **425** and/or a well of sample carrier **115** so as to aspirate samples and/or reagents and introduce them into flow cell **192** (the movement of fluids being controlled through pump **870**, the selection of reagents aspirated from fluid handling ~~manifold~~ system **425** being controlled by valves **470** and sensors **500** operating so as to send an error message if a reagent line becomes empty). Optionally, pipettor **405** may also be used to combine samples and/or reagents into an incubation chamber (e.g., to carry out assay reactions prior to introduction of samples into flow cell **192**). The incubation chamber may be, e.g., a well of sample carrier **115** or an additional system component.

Please replace the paragraph beginning at page 19, line 19, with the following paragraph:

Assay measurements are conducted on samples and/or assay reaction mixtures in flow cell **192**. Computer system **101** receives data and, preferably, carries out data analysis. After completion of a measurement, the flow cell is preferably cleaned and prepared for the next measurement. The cleaning process may include the introduction of cleaning reagents into flow cell **192** by directing pipettor **405** and pump **870** to aspirate cleaning reagents from fluid handling ~~manifold~~ system **425** or sample carrier **115**.

Please replace the paragraph beginning at page 35, line 9, with the following paragraph:

By way of example, **Fig 1a** shows a flow cell based assay system that includes a probe **150** for aspirating samples and reagents from microtiter plate **115** and/or fluid handling ~~manifold~~ system **425**. [[Probe]] Pipettor 405 and probe **150** [[is]] are moved using a motion control system that controls [[a]] z-axis actuator **177** that moves the probe in the direction perpendicular to the plate and one or more actuators that move the probe along one or more paths parallel to the plate. These paths can be any arbitrary shape but are preferably linear or radial; **Fig. 1a** shows two linear actuators for moving the probe along paths parallel to the plate, [[an]] x-axis actuator **176** and [[a]] y-axis actuator **175**. Linear actuators are, preferably, driven by motors such as DC motors or stepper motors and are, more preferably, based on motor driven ball screw, acme screw or belt drive assemblies, and are most preferably driven by stepper motors. Optionally, the motion control system may include one or more sensors (e.g., position sensors, contact sensors, encoders such as optical encoders, pressure sensors, limit switches, etc.) that report the position of the probe along one or more degrees of freedom or detect when the probe hits a defined position or reaches the limit of travel along one or more degrees of freedom.

Please replace the paragraph beginning at page 45, line 7, with the following paragraph:

Turning to **Figs. 4a** and **4b**, a fluid handling ~~station~~ system [[**400**]] **425**, comprising a subsystem of the fluid handling device **471**, can be employed and configured, in accordance with one preferred embodiment, to supply to a [[probe]] pipettor **405**, that may be comprised of a combination of components including a fluidic probe **150** (e.g., a pipettor, pipet tip, syringe needle, cannula, etc.), the appropriate liquids through an access, or dispense, port **455** for aspiration into the flow cell. ~~A fluidic probe~~ Pipettor **405** ~~(e.g., a pipettor, pipet tip, syringe needle, cannula, etc.)~~ may be used to access an aspiration chamber **450** of the fluid handling ~~station~~ system [[**400**]] **425** at port **455** to aspirate the appropriate liquids. Aspiration chamber **450** is connected to reagents through reagent lines **430** and **435** and reagent valves **431** and **436** and to [[air]] a gas through [[air]] gas line **440** and valve **441**. In one embodiment, the aspiration chamber **450** may be substantially the same height as probe **150** when measured independently. [[Probe]] Pipettor **405** can be sealed against fluid handling ~~station~~ system [[**400**]] **425** to form a closed system, preferably by utilizing a face sealing configuration located above the reagent inputs.

Please replace the paragraph beginning at page 45, line 17, with the following paragraph:

Figs. 4a-c depict one preferred embodiment of a fluid handling ~~station~~ system employing a face seal. A face seal, as defined herein, is a seal formed using at least one sealing surface placed in contact with an opposing surface and is illustrated as face seal **460** in Fig. **4a**. Probe [[**405**]] **150** is inserted into aspiration chamber **450** of the body of fluid handling ~~station~~ system

[[body]] **425**. Preferably, the [[probe]] pipettor **405** is configured with a sealing surface **410**, e.g., flange, shoulder, collar, or the like, that is brought into sealing relation with a sealing surface **415** of the body of fluid handling ~~station~~ system [[body]] **425**. Preferably, one of the sealing surfaces **410** or **415**, most preferably sealing surface **415**, comprises a gasket or o-ring for forming a fluid and air tight seal. In one embodiment, the o-ring or gasket is partially inset into a sealing surface of the body of fluid handling ~~station~~ system [[block]] **425** leaving at least some portion of the o-ring, adequate for a compression seal, exposed above [[the]] a face surface of the fluid handling ~~station~~ system [[block]] **425**. Insetting the o-ring or gasket into an appropriate groove, for example, groove **417**, will provide physical retention and prevent dislodgement during operation.

Please replace the paragraph beginning at page 46, line 5, with the following paragraph:

In operation, the probe is lowered to form the face seal in order to aspirate reagents, more preferably, the lowering comprises compressing sealing surface **410** against sealing surface **415** so as to form a compression seal. Preferably the reagent level **422** of liquid reagent **420** is maintained so that when the [[probe]] pipettor **405** is lowered into position in the aspiration chamber **450**, the volume of the probe **150** displaces the reagent level **422** so that it is slightly above the reagent input lines **430**, **435** for the liquid reagents. This configuration allows the [[probe]] pipettor **405**, when properly positioned within the aspiration chamber **450**, to form a closed system for drawing (i.e., sucking, pumping, etc.) the reagents from the reagent input lines **430**, **435** which are controlled by valves **431** and **436**.

Please replace the paragraph beginning at page 46, line 15, with the following paragraph:

During aspiration of reagents, the tip of probe [[**405**]] **150** is, advantageously, lower than reagent lines **430** and **435** so that the flow of reagents efficiently cleans the probe surface and washes away any previous reagents that were held in aspiration chamber **450**. This cleaning and washing effect is especially efficient if aspiration chamber **450** is only slightly larger in width or diameter (preferably less than 100% large, more preferably less than 50% larger, most preferably less than 20% larger) than probe [[**405**]] **150**. In addition, it is preferable to arrange and configure the entry points of the reagent input lines **430**, **435** so that their fluid paths enter the aspiration chamber **450** at substantially the same height as one another. This provides an additional advantage for proper flushing between reagents.

Please replace the paragraph beginning at page 47, line 1, with the following paragraph:

[[Air]] Gas line **440** is preferably arranged sufficiently above the liquid reagent lines **430**, **435** in order to maintain a vertical separation between the [[air]] gas line **440** and the liquid reagent lines **430**, **435**. The gas provided through gas line **440** may, for example, be air. Advantageously, this reduces or eliminates the contamination of the [[air]] gas lines **440** with liquid reagents. It also allows the aspiration of a bolus of air into the probe to be used to clear excess reagent from aspiration chamber **450** and/or to prevent mixing of reagents in the probe or subsequent fluid lines (i.e., by separating the reagents in the fluid lines into so-called "slugs" of fluid separated by boluses of air).Paragraph beginning at page 47, line 19

Please replace the paragraph beginning at page 47, line 19, with the following paragraph:

As can be seen in **Fig. 4b**, raising the probe **150** and pipettor **405** out of aspiration chamber **450** does not lead to wetting of the seal **415**. Instead, the o-ring seal **415** remains dry as the [[probe]] pipettor **405** is raised due to the lowering of reagent level **422**. To reduce the reagent level **422** further, the system can aspirate through the probe [[**405**]] **150** as the probe is being raised. Optionally, fluid can also be drawn into the probe [[**405**]] **150** as the [[probe]] pipettor **405** is lowered to further reduce mixing of reagents during transitions.